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EXAMINER

LAM, ANN Y

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/529,197	<b>Applicant(s)</b> HASELTON ET AL.	
	<b>Examiner</b> ANN Y. LAM	<b>Art Unit</b> 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 25 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3-39 and 70-116 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1 and 3-39 is/are allowed.
- 6) ☒ Claim(s) 79, 81, 84-116 is/are rejected.
- 7) ☒ Claim(s) 80,82 and 83 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

***Election/Restrictions***

***Claim Objections***

Claims 4-6 and 82-83 are objected to because of the following informalities: these claims recite “different probes” but it appears that Applicant intends for the phrase to mean --different types of probes--. Applicant should thus amend the claims to use the latter language for clarity. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 87, 97 and 99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 87, line 1 recites “the post-processing”. There is insufficient antecedent basis for this limitation.

Claim 97 depends from claim 99, but claim 99 depends from claim 97. Thus both claims 97 and 99 are unclear. It appears that Applicant meant for claim 97 to depend from claim 79 and thus will be interpreted as such for examination purposes.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 79, 81, 84-86, 89, 91-105 and 107 are rejected under 35 U.S.C. 102(e) as being anticipated by Huang et al., 7,015,047.

As to claim 79, Huang et al. teach magnetizable microdevices (col. 17, lines 8-9), having binding partners capable of binding to a moiety to be detected (col. 20, lines 25-27), wherein the microdevices are used to bind to a moiety and to manipulate the moiety (col. 34, lines 19-21) and to detect the moiety by detecting the photorecognizable coding patterns, such as barcodes or fluorescence (col. 19, lines 1-7.) For example the microdevices can have antibodies immobilized thereon to capture and bind to target cells (col. 20, lines 49-52.) The microdevices can be rod-shape (col. 43, lines 39-46), which is deemed to be a filament because it has the same shape as a filament, i.e., cylindrical, elongated element. The microdevices are deemed to be traversing through a first chamber, wherein the first chamber contains the target in solution because the microdevices are flowing within a flow system (col. 40, line 3-11.) The binding partner on the microdevices are deemed to be the first probe. The detection step is deemed to be the step of assessing binding.

As to claim 81, Huang et al. teach that the optical labeling substance used is a fluorescence substance or bar code (col. 18, line 64 – col. 19, line 5). The binding partner on the microdevice is deemed to be associated with the fluorescence substance or bar code, i.e., the probe identifier.

As to claims 84 and 85, Huang et al. teach a step of collecting the microdevice through an outlet channel. The outlet channel is deemed to be a second chamber, which lacks the target. The outlet channel is also considered to be used for post-processing, since it provides for removal of materials after the detection steps.

As to claim 86, Huang et al. teach introducing a liquid suspension in order to form an array of microdevice (col. 34, line 59- col. 35, line 13.)

As to claim 89, the probe identifier is a bar code (col. 18, line 64 – col. 19, line 5).

As to claim 91, the bar code is disposed in a linear fashion (see fig. 8 and col. 5, lines 32-39.)

As to claim 92, Huang et al. teach that thermal convection may be used to facilitate liquid mixing (col. 29, lines 11-22.)

As to claim 93, Applicants do not specify what the surface features are and thus the sides of the rod-shape microdevices (col. 43, lines 39-46), which is deemed to be a filament.

As to claim 94, Applicants do not specify what the surface features are and thus the walls of the flow channel are deemed to be the claimed surface features because they enhance mixing by confining the solution.

As to claim 95, the filament is transparent (col. 43, lines 62-65 and lines 42-45.)

As to claim 96, Huang et al. teach that metal films made of gold for example can be incorporated into the microdevices and increase electrical conductivity of the microdevices (col. 14, lines 58-61.)

As to claim 97, the target is subject to electrophoretic movement (col. 12, 1-11).

As to claim 98, the electrophoretic movement promotes target-probe interaction (col. 15, lines 36-44.)

As to claim 99, use of electrophoretic movement by a skilled artisan to for example remove unbound target or probe, as is well known in the assay art to allow for detection of the bound target, is equivalent to inhibiting target-probe interaction.

As to claim 100, the manipulation of the microdevice through one portion of a channel of flow device is considered to be the first traversing through a chamber, and the manipulation through the next portion of the channel is considered to be the second traversing, since Applicants have not provided any limitations regarding the structure of the chamber.

As to claim 101, Huang et al. teach that manipulation of moieties include separation of moieties, using compatible means disclosed, such as electrophoretic (col. 15, lines 24-28.)

As to claim 102, the manipulation of the microdevice through the next portion of the channel is considered to be a second traversing in a different chamber.

As to claim 103, Huang et al. teach that directed thermal convection may act as an active force (col. 29, lines 21-22.) Thus, with directed thermal convention, the temperature in one part of the flow system is different from another part.

As to claims 104 and 105, with electrophoresis being the means to manipulate moieties (col. 15, lines 24-28), the charge or voltage in one part of the flow system (i.e., one chamber) is different or altered from that in another part.

As to claim 107, the optical labeling with a fluorescence substance or bar code (col. 18, line 64 – col. 19, line 5) is considered to be enhancing detection of binding of the target to the first immobilized probe.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 113-116 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al., 7,015,047.

As to claim 113, Huang et al. do not disclose the diameter of the rod. However, Huang et al. do teach that the microdevice can be in any suitable shape and dimension and have thickness from about 0.1 micron to about 500 microns (col. 17, lines 37-43.) It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. (MPEP 2144.05 IIA, citing *In re Aller*, 105 USPQ 233). In this case, Huang et al. disclose the

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general conditions of the claim and the diameter of the rod being in the range claimed by Applicant is a workable or optimum range and thus its discovery involves only routine skill in the art.

As to claim 114, Huang et al. also do not disclose the diameter of the processing chamber. However, the diameter claimed by Applicants is within a workable or optimum range and thus its discovery involves only routine skills in the art given that Huang et al. disclose the general conditions of the claim.

As to claim 115, Huang et al. also do not disclose the volume of the target solution, but the range in volume recited by Applicants is within a workable or optimum range and thus its discovery involves only routine skill in the art given that Huang et al. disclose the general conditions of the claim.

As to claim 116, Huang et al. do not teach that the probe density of the filament. However, such probe density is within a workable range and thus its discovery involves only routine skills in the art.

Claim 90 is rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al., 7,015,047, in view of Connell, 3,818,444.

Huang et al. disclose the invention substantially as claimed (see above) except for the bar code being in an annular fashion. Huang et al. rather disclose linear bar codes (see fig. 8).



Connell however teach that the omni-directional reading characteristics of an annular bar code can be read by any directional scanning beam intersecting the common center (col. 1, line 57-61.) It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide a bar code in the Huang et al. microdevice in an annular fashion because Connell disclose that annular bar codes provide the benefit of reading the code in any directional scanning beam intersecting the common center, as would be desirable for convenience.

Claims 87, 88, 101, 106 and 108-112 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al., 7,015,047, in view of Kayyem et al., 2002/0006643.

Huang et al. disclose the invention substantially as claimed except for a second liquid phase probe that binds to the target at a location distinct from the first probe and a third liquid phase probe that is in an inactive state and then activated to facilitate amplification.

However Kayyem et al. teach amplification of target nucleic acid sequence using branched or linear conformation and using label probes that hybridize to the amplification sequences (paragraph 0174). The invention includes an amplifier probe, i.e., a nucleic acid probe that is used to facilitate signal amplification (paragraph 0176.) Amplifier probes may have a first probe sequence that is substantially complementary to a portion of an additional probe, in this case called a label extender probe, that has a

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first portion that is substantially complementary to the target sequence (paragraph 0177.) In a preferred embodiment, the amplifier probes, or any of the other probes of the invention, may form hairpin stem-loop structures in the absence of their target (paragraph 0179.) Generally, these hairpin structures comprise four components, including a third component that is a self-complementary region, which has a first portion that is complementary to a portion of the target sequence region and a second portion that comprises a first portion of the label probe binding sequence. The fourth component is substantially complementary to a label probe (or other probe, as the case may be), (paragraph 0180.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the nucleic acid sequences, and labeling and detection technique disclosed by Kayyem et al. in the Huang et al. invention because Kayyem et al. teach that they provide the benefit of amplification of the target nucleic acid sequence as would be desirable for more accurate detection.

As to claims 108, 109, 111 and 112, the label extender probe is equivalent to the second liquid phase. The amplifier probe is equivalent to the claimed third liquid phase, having a binding site(s) for itself (since it has a component that is self—complementary.)

As to paragraph 110, the label may be a fluorescent label (Kayyem et al., paragraph 0413.)

As to claim 87, Huang et al. do not disclose a post-processing step comprising deblocking of a reactivating group on a target. However Kayyem et al. provides the motivation to modify the Huang et al. invention as discussed above. Kayyem et al. also

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teach that once the hybridization complex is formed, and the cross-linking agent has been activated such that the primers have been covalently attached, the reaction is subjected to conditions to allow for the disassociation of the hybridization complex, thus freeing up the target to serve as a template for the next ligation or cross-linking. In this way, signal amplification occurs, and can be detected (paragraph 0116.) The disassociation is equivalent to the pos—processing step claimed.

As to claim 88, Huang et al. do not disclose that the target is labeled with a fluorescent label. However given the modifications to the Huang et al. invention as suggested by Kayyem et al. as discussed above, the target is labeled with a fluorescent label, as Kayyem et al. disclose that the label may be a fluorescent label (paragraph 413.)

As to claims 101 and 106, Huang et al. do not teach traversing a second time through the first chamber or recirculating the target solution. However, Kayyem et al. teach repeating amplification steps depending on the sensitivity of the detection (paragraph 0083). The skilled artisan would thus repeat the amplification discussed above, and would modify the Huang et al. invention such that a recirculation occurs to repeat the amplification through the device.

### ***Allowable Subject Matter***

Claims 1 and 3-39 are allowed.

Claims 80, 82 and 83 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: the prior art does not teach providing probes in an annular fashion around a particle or filament. The prior art also does not teach providing a plurality of different types of probes on a particle or filament for probe-target interaction. The prior art uses different beads with different probes but with each bead having *identical* probes and attached labels (see for example Brenner RE 39793, claim 5). Applicant's claimed invention (in claims 82 and 83) uses a filament as a solid support with *different* probes on a *single* filament, and such an embodiment is not disclosed in the prior art, nor does the prior art provide a reason for the skilled artisan to depart from the known embodiment.

### ***Response to Arguments***

Applicant's claims 79-116 were added to reflect the original claims, most of which had been rejected over Huang et al. in the first Office action. The previous Office action had indicated that some of these claims are allowable, but upon a review, these claims are still deemed to be not patentable over Huang et al. for the reasons set forth above.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/  
Primary Examiner, Art Unit 1641